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In the Supreme Court of the United States

TOMMY G. THOMPSON,
SECRETARY OF HEALTH AND HUMAN SERVICES,
ET AL., PETITIONERS

v.

WESTERN STATES MEDICAL CENTER, ET AL.

ON WRIT OF CERTIORARI
TO THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

REPLY BRIEF FOR THE PETITIONERS

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25pp

TABLE OF CONTENTS

	Page
1. Section 353a furthers substantial governmental interests	3
2. Section 353a directly and materially advances the government's interests	16
3. Section 353a is no more extensive than necessary to further the government's interests	17

TABLE OF AUTHORITIES

Cases:

Alberty Food Prods. v. *United States*, 194 F.2d 463 (9th Cir. 1952)	13
Baker v. *United States*, 932 F.2d 813 (9th Cir. 1991)	15
Cedars North Towers Pharmacy, Inc. v. *United States*, [1978-1979 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200 (S.D. Fla. Aug. 28, 1978)	9, 10
Central Hudson Gas & Elec. Corp. v. *Public Serv. Comm.*, 447 U.S. 557 (1980)	1, 16
Dolan v. *City of Tigard*, 512 U.S. 374 (1994)	20
44 Liquormart, Inc. v. *Rhode Island*, 517 U.S. 484 (1996)	18, 19, 20
International Union of Operating Eng'rs v. *Flair Builders, Inc.*, 406 U.S. 487 (1972)	8
Kadis v. *United States*, 373 F.2d 370 (1st Cir. 1967)	9
Lorillard Tobacco Co. v. *Reily*, 533 U.S. 525 (2001)	16
Marks v. *United States*, 310 F.2d 49 (5th Cir. 1962)	9
Pittsburgh Press Co. v. *Human Relations Comm'n*, 413 U.S. 376 (1973)	19

Case—Continued: Page

Posadas de Puerto Rico Assoc. v. *Tourism Co.*, 478 U.S. 328 (1986) 16
Professionals & Patients for Customized Care v. *Shalala*, 56 F.3d 592 (5th Cir. 1995) 10, 15
Rubin v. *Coors Brewing Co.*, 514 U.S. 476 (1995) 18, 19
Rush v. *United States*, 370 F.2d 520 (8th Cir. 1967) 9
United States v. *Algon Chem., Inc.*, 879 F.2d 1154 (3d Cir. 1989) 10, 13
United States v. *Arnold's Pharmacy*, 116 F. Supp. 310 (D. N. J. 153) 9
United States v. *Articles of Drug*, 625 F.2d 665 (5th Cir. 1980) 13
United States v. *Baxter Healthcare Corp.*, 712 F. Supp. 1352 (N.D. Ill. 1989) aff'd 901 F.2d 1401 (7th Cir. 1990) 13
United States v. *Carlisle*, 234 F.2d 196 (5th Cir. 1956) 9
United States v. *Dianovin Pharm., Inc.*, 475 F.2d 100 (1st Cir.), cert. denied, 414 U.S. 830 (1973) 15
United States v. *Edge Broad. Co.*, 509 U.S. 418 (1993) 16
United States v. *Gibson*, 135 F. Supp. 807 (E.D. Pa. 1955) 9
United States v. *9/1 Kg. Containers*, 854 F.2d 173 (7th Cir. 1988) 10, 13
United States v. *Rutherford*, 442 U.S. 544 (1979) 13
United States v. *Sene X Eleemosynary Corp.*, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. Jan. 12, 1983) 5, 9, 10
United States v. *Sullivan*, 332 U.S. 689 (1948) 9
Virginia State Bd. of Pharmacy v. *Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748 (1976) 12, 18, 19
Weinberger v. *Hynson, Westcott, & Dunning, Inc.*, 412 U.S. 609 (1973) 11

Constitution, statutes and regulations: Page

U.S. Const. Amend. I 1, 19, 20
Act of June 25, 1938, ch. 675, § 291(p)(1), 52 Stat. 1041 11
Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 11
Federal Food Drug and Cosmetic Act, 21 U.S.C. 301 *et seq.* 1
21 U.S.C. 321(g)(1)(D) 14
21 U.S.C. 321(p)(1) 7, 8
21 U.S.C. 331(d) 12
21 U.S.C. 331(k) 14
21 U.S.C. 351(a)(2)(B) (1994 & Supp. V 1999) 14
21 U.S.C. 352(f) 14
21 U.S.C. 352(f)(1) 13
21 U.S.C. 353(b)(1)(B) (1994 & Supp. V 1999) 13
21 U.S.C. 353(b)(2) 13
21 U.S.C. 353a (Supp. V 1999) ..... *passim*
21 U.S.C. 353a(a) (Supp. V 1999) 1, 7
21 U.S.C. 353a(a)(2)(A) (Supp. V 1999) 14
21 U.S.C. 353a(c) (Supp. V 1999) 1, 19
21 U.S.C. 355 7
21 U.S.C. 355(a) 7, 12
21 U.S.C. 360(a)(1) 8
21 U.S.C. 360(b)-(d) 8
21 U.S.C. 360(g)(1) 8
21 U.S.C. 374(a)(2)(A) 8
21 U.S.C. 374(a)(1) 9
21 U.S.C. 501(a)(2)B 15
21 U.S.C. 505 15
21 U.S.C. 502(f)(1) 15

Statutes and regulations—Continued:

Mont. Code Ann. (2001):
§ 37-7-101(7) 5
§ 37-7-101(17) 5

Statutes and regulations—Continued:	Page
Ohio Rev. Code Ann. § 3715.01(14) (Anderson 2001)	5
Tex. Occ. Code Ann. (West 2001):	
§ 551.003(9)	5
§ 551.003(23)	5
21 C.F.R. 130.39 (1968)	12
21 C.F.R. (2001):	
Pt.:	
Section 201.5	13
Section 201.100 *et seq.*	14
Pt. 210	14
Pt. 211	14
Miscellaneous:	
ASHP Gears Up Multistate Action Plan Regarding Sterile Drug Products, 48 Am. J. Hosp. Pharm. 386 (1991)	4
J. Avorn, et al., *Scientific versus Commercial Source of Influence on the Prescribing Behavior of Physicians*, 73 Am. J. of Med. 4 (July 1982)	17
17 Fed. Reg. 6818 (1952)	13
33 Fed. Reg. 7758 (1968)	12
J. Feinberg, *Compounding Sterile Products: What is Good Pharmacy Practice?*, 7 The Consultant Pharmacist 1012 (1992)	4
H.R. Conf. Rep. No. 399, 105th Cong., 1st Sess. (1997)	15
R. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 Va. L. Rev. 1753 (1996)	11
NAPB, *The Model State Pharmacy Act and Model Rules of the NAPB* (1996)	5
J. O'Donnell, *Cardioplegia Litigation and Recommendations*, 6 J. Pharm. Practice 151 (1993)	4
S. Rep. No. 43, 105th Cong., 1st Sess. (1997)	15
L. Trissel, *Compounding Our Problems*, 51 Am. J. Hosp. Pharm. 1534 (1994)	4

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REPLY BRIEF FOR THE PETITIONERS

The Food and Drug Administration Modernization Act of 1997 (FDAMA) creates a limited exemption from the requirements of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 301 *et seq.*, governing the approval of new drugs, adequate directions for use, and good manufacturing practice for drugs compounded by pharmacists. See 21 U.S.C. 353a (Supp. V. 1999). The exemption is contingent on the pharmacist's compliance with various conditions, including that the pharmacist not solicit prescriptions for, advertise, or promote any particular compounded drug or class of compounded drug. 21 U.S.C. 353a(a) and (c) (Supp. V 1999). That condition is consistent with the First Amendment under *Central Hudson Gas & Electric Corp.* v. *Public Service Commission*, 447 U.S. 557 (1980).

Section 353a is designed to advance the substantial governmental interest in balancing two important but competing goals. The first goal is to safeguard the integrity of the FDCA's new drug approval process, which protects the public from the health risks of widespread distribution of drugs that have not been proven safe and effective. See Pet. Br. 19-23. The second is to make compounded drugs available when necessary to meet the particularized medical needs of individual patients. See *id.* at 23-26. Those goals are in tension with each other but that tension may be accommodated and reconciled: It typically is not feasible to subject drugs compounded by a pharmacy in response to individual medical needs to the expensive premarket approval process. *Id.* at 26-27. At the same time, a blanket exemption from that process for anyone holding a pharmacy license would undermine the process by allowing drugs to be mass-produced outside the stringent regulatory framework established by Congress, and, by thereby reducing the incentive for other manufacturers to establish the safety and effectiveness of their products. *Id.* at 28-29.

The solicitation and advertising conditions thus directly advance the government's interest in balancing those competing goals. Promotion of particular drugs reasonably distinguishes large-scale drug manufacturing, which can and should be subject to premarket approval, from compounding in response to the particularized medical needs of specific individuals. See Pet. Br. 32-35. Conditioning the exemption from the approval requirements on the absence of promotion of particular drugs also reflects the FDCA's underlying premise that the public health is best served when those who develop, promote, and mass-distribute new drugs prove that they are safe and effective. Because all persons who compound new drugs (whether traditional manufacturers or those holding a pharmacy license) are unable to promote specific products through advertising unless they comply

with the approval process, they are unable to take advantage of a mass-market without complying with the process. The integrity of the process and the incentive for drug manufacturers to prove that the drugs that they distribute in interstate commerce are safe and effective are thereby preserved. *Id.* at 35-36. The advertising and solicitation limitations are thus carefully crafted to meet the government's goals. See *id.* at 42-46.

1. Section 353a Furthers Substantial Governmental Interests

a. Respondents contend (Br. 18-23) that the government has not established a substantial interest in subjecting compounding that is tantamount to manufacturing to the new drug approval process. They first argue (Br. 18, 20-21) that the government has not adequately and properly delineated the difference between compounding and manufacturing. The government's opening brief, however, differentiates between the two processes in terms similar to those used by the National Association of Boards of Pharmacy (NABP) itself. See Pet. Br. 33-35 & n.6. Traditional compounding involves the provision of a service in response to a physician's prescription and the particular medical needs of an individual patient that cannot be met by commercially available products. *Id.* at 33. Because traditional compounding responds to idiosyncratic medical needs of specific individuals, advertising of particular compounded drug products is not one of its necessary or common characteristics. *Id.* at 33-34. Manufacturing, in contrast, is the large-scale production of a drug product, typically for a substantial market that can support the expense and other rigors of the premarket approval process. Because manufacturing involves creation of a homogenous product that addresses the shared medical need of a large group of people, advertising of that product is one of its common and typically critical features. See *id.* at 34-35.

Respondents argue (Br. 21-22, 30, 44) that the widespread distribution of unapproved compounded drugs is not harmful. The very premise of the FDCA, however, is that widespread distribution of drugs that have not been proven safe and effective poses substantial risks to public health and that premarket approval is necessary to protect against those risks. See Pet. Br. 23, 30. That premise is supported by many decades of experience showing that neither the self-interest of drug producers nor physician screening is sufficient to protect the public. See *id.* at 20-23. The widespread distribution of unapproved new drugs threatens the integrity of the drug approval process and the public health whether or not the manufacturer has a pharmacy license under state law. See *id.* at 27-29.[1]

Respondents (Br. 12, 20) and amicus National Community Pharmacists Association (NCPA) (Br. 24-25) also contend that advertising of particular drugs does not reasonably distinguish manufacturing from traditional compounding. As just described, however, promotion of the manufactured product is a common and typically critical feature of commercial drug manufacturing, but not of traditional compounding. Indeed, NABP's Model State Pharmacy Act distinguishes between manufacturing and compounding based on the presence or absence of promotional activity. Compare § 105(u) (defining "manufacturing" to include "the promotion and

[1] Although respondents assert (Br. 30) that the government has offered only "one anecdotal incident" documenting the health risks from drugs compounded by pharmacists, the articles cited in the government's opening brief (at 28) discuss several incidents, and there is ample additional documentation of these risks. See, *e.g.*, *ASHP Gears Up Multistep Action Plan Regarding Sterile Drug Products*, 48 Am. J. Hosp. Pharm. 386 (1991); J. Feinberg, *Compounding Sterile Products: What is Good Pharmacy Practice?*, 7 The Consultant Pharmacist 1012, 1013 (1992); J. O'Donnell, *Cardioplegia Litigation and Recommendations*, 6 J. of Pharm. Practice 151, 151-152 (1993); L. Trissel, *Compounding Our Problems*, 51 Am. J. Hosp. Pharm. 1534 (1994).

marketing" of drugs) with § 105(e) (omitting promotion and marketing from definition of compounding) (*reprinted in* NABP, *The Model State Pharmacy Act and Model Rules of the NABP* 1.2, 1.4 (1996)). Many state laws draw a similar distinction. See Am. Pharm. Ass'n (APhA) Amicus Br. 15 n.19 (citing 10 state statutes); Mont. Code Ann. § 37-7-101(7) and (17) (2001); Ohio Rev. Code Ann. § 3715.01(14) (Anderson 2001); Tex. Occ. Code Ann. § 551.003(9) and (23) (West 2001). Moreover, the NABP's *Good Compounding Practices Applicable to State Licensed Pharmacies* prohibit a pharmacist from soliciting prescriptions for, advertising or otherwise promoting specific compounded drugs. NABP, *supra*, at App. C.2.

b. Respondents argue (Br. 12, 19-20, 29) that the government lacks a substantial interest in preventing manufacturing under the guise of pharmacy compounding because "compounding can never be manufacturing and manufacturing can never be compounding." *Id.* at 19. Respondents assert (*ibid.*) that pharmacy compounding differs from manufacturing because drugs compounded by pharmacists are dispensed directly to patients based on prescriptions arising from physician/patient/pharmacist relationships. Those characteristics do not, however, distinguish compounding from large-scale drug production that can and should be subject to premarket approval. Pharmacies (or traditional manufacturers that form entities with a pharmacy license) could still "compound" new drugs in the manner of traditional manufacturing even if they dispensed the drugs pursuant to patient prescriptions. In *United States* v. *Sene X Eleemosynary Corp.*, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207 (11th Cir. Jan. 12, 1983), for example, the "pharmacy" dispensed the drugs it produced pursuant to prescriptions for individual patients. The court nonetheless concluded that the "pharmacy" was manufacturing, *id.* at 39,118, and respondents agree (Br. 41).

Under respondents' theory, nothing would prevent a "compounding pharmacy" from producing the next Prozac and marketing it nationwide to millions of individuals, without first proving the drug's safety and effectiveness to the FDA, provided only that the pharmacy made its sales pursuant to prescriptions mailed or telephoned in by physicians. Thus, respondents' approach would allow wholesale circumvention of the drug approval process and seriously undermine the FDCA's central mechanism to protect the public at large from the risks of drugs that have not been proven safe and effective.

Respondents assert, without support, that, "if and when demand for a compound ever increases to a level where manufacturing becomes practical (*i.e.*, profitable), a manufacturer may bring it to market, whereupon pharmacies will stop making it." Resp. Br. 19. If, however, pharmacies were already meeting the demand for a product through compounding, and doing so without bearing the costs of FDA approval, there would be little incentive for a prospective manufacturer to undertake the expense of obtaining FDA approval, particularly if pharmacies could sell the product at a lower price because they do not have to recoup the costs of the approval process. Further, if pharmacies knew that they could sell the drug at a lower price and thus enjoy an advantage over potential competitors, the pharmacies would be unlikely to give up their existing, profitable business.

c. Respondents and their amici proffer one additional reason why the government purportedly lacks a substantial interest in preventing circumvention of the new drug approval process: They assert that drugs compounded in the ordinary practice of pharmacy are not subject to the approval process in the first place and thus may legally be introduced into interstate commerce or held for sale without FDA approval. See Resp. Br. 3, 12-14, 16, 29, 34-45, 46; Amicus Br. of Int'l Academy of Comp. Pharm. (IACP) 2-22; NCPA Br. 10-15; APhA Br. 20-24.

i. As an initial matter, compounded drugs are not exempt from the new drug approval requirements. If they were, Congress would have had no need to create the exemption from those requirements that Section 353a provides. See 21 U.S.C. 353a(a) (Supp. V 1999) (stating that Section 355, which contains the approval requirements, "shall not apply" to compounded drugs under specified conditions). Thus, the enactment of Section 353a itself establishes that compounding by pharmacists is otherwise covered by the new drug approval requirements.

As explained in the government's opening brief (at 4), compounded drugs fall within the definition of a "new drug" in 21 U.S.C. 321(p)(1). They are thus subject to the approval requirements, which provide that "*[n]o person* shall introduce or deliver for introduction into interstate commerce *any new drug*" without prior FDA approval. 21 U.S.C. 355(a) (emphasis added). Neither respondents nor their amici identify any provision of the FDCA that exempts drugs compounded by pharmacies from the definition of new drug or the approval requirements.[2]

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[2] Respondents incorrectly assert (Br. 12, 16, 34-35) that the government conceded in the court of appeals that introduction of compounded drugs into interstate commerce without FDA approval is legal. The government took the same position in that court that it takes here: Because Section 353a itself provides that introduction of compounded drugs into interstate commerce without FDA approval is legal under carefully circumscribed conditions, the government did not and does not argue that respondents' proposed advertisements of compounded drugs concern illegal activity under the first component of the *Central Hudson* test. See Pet. Br. 18; Appellants Br. 27 n.10. That does not mean, however, that introduction of unapproved compounded drugs into interstate commerce, or holding such drugs for sale, was legal before FDAMA, or is legal today absent compliance with the conditions in Section 353a. On the contrary, as the government's court of appeals' brief stated, "before

Respondents argue that compounded drugs are not "mentioned or included in" the definition of "new drug." Br. 4; see *id.* at 35, 37, 39. That definition, however, includes "*[a]ny* drug" that "is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use." 21 U.S.C. 321(p)(1) (emphasis added). The use of the modifier "any" eliminates the need explicitly to include drugs compounded by pharmacists. See *International Union of Operating Eng'rs* v. *Flair Builders, Inc.*, 406 U.S. 487, 491 (1972). Respondents do not contend that compounded drugs are generally recognized among experts as safe and effective. Indeed, respondents argue (Br. 35-37) that compounded drugs are not new drugs precisely because they are (according to respondents) incapable of being evaluated by experts. That fact, if true, however, demonstrates the opposite proposition—that compounded drugs necessarily are "new drugs."

ii. Respondents also argue more broadly (Br. 4, 8, 13, 37-40) that pharmacies are entirely exempted from the FDCA by 21 U.S.C. 360(a)(1), 360(g)(1), and 374(a)(2)(A). Section 360(a)(1), however, provides no exemption from any provision of the FDCA for any entity. Rather, it stipulates that repackaging or relabeling constitutes "manufacture, preparation, propagation, compounding, or processing" that generally subjects the person engaged in such conduct to the registration requirements contained in Section 360(b)-(d). Section 360(g)(1) exempts pharmacies that engage in only the ordinary pharmacy practice of dispensing or selling drugs at retail from registration requirements, and Section 374(a)(2)(A) exempts such pharmacies from certain (but not

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Congress enacted FDAMA in 1997, the FDCA did not exempt compounding from the Act's new drug, adulteration, and misbranding requirements," *id.* at 27, and "the interstate distribution of any compounded drug product without approval was illegal." *Id.* at 31.

all) of the inspection requirements in Section 374(a)(1). Those provisions do not, however, exempt pharmacies from any *other* provisions of the FDCA, including those governing new drug approval, misbranding, and adulteration. Pet. Br. 3. Indeed, the existence of express exemptions from the registration and inspection requirements confirms that pharmacies are generally subject to the FDCA and that they are *not* exempt (except to the extent expressly provided in Section 353a) from those other requirements.

iii. Respondents claim that the FDA has demonstrated a "complete lack of regulation or enforcement activity towards pharmacies." Br. 14. That claim cannot be reconciled with *United States* v. *Sullivan*, 332 U.S. 689 (1948), in which this Court upheld a misbranding action brought against a pharmacist less than a decade after the FDCA was enacted. See also *Kadis* v. *United States*, 373 F.2d 370 (1st Cir. 1967); *Rush* v. *United States*, 370 F.2d 520 (8th Cir. 1967); *Marks* v. *United States*, 310 F.2d 49 (5th Cir. 1962); *United States* v. *Carlisle*, 234 F.2d 196 (5th Cir. 1956); *United States* v. *Gibson*, 135 F. Supp. 807 (E.D. Pa. 1955); *United States* v. *Arnold's Pharmacy*, 116 F. Supp. 310 (D.N.J. 1953). As described in the 1992 Compliance Policy Guide (CPG) on compounding, the FDA has long taken the position that drugs compounded by pharmacies are subject to the new drug approval requirements. See Pet. Br. 4-5; Pet. App. 71a, 72a (CPG). Respondents and some amici mistakenly contend (Resp. Br. 25, 43; ICPA Br. 5, 14; NCPA Br. 12) that the FDA had not taken that position before promulgating the CPG. The FDA made clear that compounded drugs are new drugs and subject to the approval requirements many years before the 1992 CPG. See Pet. App. 74a; Pet. Br. 6 (citing *Sene X* and *Cedars North Towers Pharmacy, Inc.* v. *United States*, [1978-1979 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200, at 38,828 (S.D. Fla. Aug. 28, 1978), in which the FDA successfully contended that drugs com-

pounded by pharmacists were subject to the approval requirements).

The government's position that compounded drugs are subject to the new drug approval requirements is supported by lower court decisions rendered well before FDAMA confirmed that coverage in 1997. See Pet. Br. 5, 6 (citing cases). Respondents and their amici (Resp. Br. 40-42; APhA Br. 17-20; IACP Br. 5 n.4; NACP Br. 12 n.44) attempt to distinguish those cases on various grounds. The facts remain, however, that, in two of the cases, the courts held that drugs compounded by pharmacies were new drugs subject to the approval process. *Sene X*, [1982-1983 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,207, at 39,118; *Cedars North Towers Pharmacy*, [1978-1979 Transfer Binder] Food Drug Cosm. L. Rep. (CCH) ¶ 38,200, at 38,827. In two others, the courts held that bulk drugs intended for use in compounding by veterinarians were not covered by a regulatory exception from the FDCA's misbranding provisions because the compounded drugs would be "new drugs" for which the veterinarians had not filed approval applications. *United States* v. *Algon Chem., Inc.*, 879 F.2d 1154, 1158 (3d Cir. 1989); *United States* v. *9/1 Kg. Containers*, 854 F.2d 173, 178 (7th Cir. 1988). And, in a fifth case, the court stated that the FDCA "does not expressly exempt 'pharmacies' or 'compounded drugs' from the new drug, adulteration, or misbranding provisions." *Professionals & Patients for Customized Care* v. *Shalala*, 56 F.3d 592, 593 n.3 (5th Cir. 1995). Respondents and their amici, on the other hand, cite no case holding that drugs compounded by pharmacists are not "new drugs" or that they are exempt from the approval requirements, and we are aware of none.

iii. Respondents' amici contend that Congress could not have subjected compounded drugs to the approval process because that would have been "tantamount to the outlawing

of compounding." APhA Br. 22; see also Resp. Br. 36-37; IACP Br. 3-4. They argue that Congress would not have outlawed compounding when it enacted the FDCA in 1938 because most prescriptions at that time required compounding. APhA Br. 21-22; IACP Br. 11; NCPA Br. 8, 11-13. That argument rests on the mistaken premise that, if all drugs compounded by pharmacists are new drugs under the current version of the FDCA, then all compounded drugs must also have been new drugs under the FDCA as enacted in 1938. In fact, most compounded drugs would not have been "new drugs" under the definition in the 1938 Act. That definition excluded drugs that had been marketed before 1938 and did not classify a drug as a "new drug" based on lack of general recognition of its effectiveness. See Act of June 25, 1938, ch. 675, § 201(p)(1), 52 Stat. 1041; Pet. Br. 21; *Weinberger* v. *Hynson, Westcott, & Dunning, Inc.*, 412 U.S. 609, 630 (1973). In addition, the 1938 Act was understood to permit the manufacture and marketing without approval of drugs similar to approved drugs in reliance on an approved "pioneer" drug application, and the FDA often issued advisory opinions that such products were not new drugs. See *id.* at 614; R. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 Va. L. Rev. 1753, 1772 (1996) (estimating that nearly 40,000 drugs similar to 4000 approved drugs were marketed without formal FDA approval before 1962).

In 1962, Congress expanded the scope of the new drug approval requirements by, among other things, expanding the definition of "new drug" to encompass drugs not generally recognized as effective for the uses prescribed, recommended, or suggested in their labeling, and requiring effectiveness to be established for each use of a new drug before the drug can be marketed for that use. See Pub. L. No. 87-781, 76 Stat. 780; Pet. Br. 22-23. In 1968, in response to the 1962 amendments, the FDA stopped providing informal

opinions that unapproved products were not new drugs, revoked all previously issued opinions, and made clear that changes "in formulation, manufacture, control, or labeling" may render a product a new drug. See 33 Fed. Reg. 7758 (1968) (codified at 21 C.F.R. 130.39 (1968)). As a result, most compounded drugs were not new drugs subject to premarket approval until the mid-1960s. By that time, less than five percent of prescriptions involved compounding. See NCPA Br. 8; *Virginia State Bd. of Pharmacy* v. *Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748, 753, 766 (1976) (estimating that the same percentage of prescriptions involved compounding in the mid-1970s). Shortly thereafter, and well before FDAMA was enacted, the FDA took formal enforcement action against some pharmacies based on failure to comply with the new drug approval requirements. See p. 9, *supra*.

The compounding and sale of new drugs by pharmacies triggered the application of the FDCA in several ways under the Act as it then existed. First, the FDCA prohibits the "introduction or delivery for introduction into interstate commerce" of any "new drug," unless it is covered by an approved new drug application. 21 U.S.C. 331(d), 355(a). Whether a local pharmacist's dispensing of a compounded drug entails or causes "introduction or delivery for introduction into interstate commerce" depends on the particular circumstances. It was less likely to do so in the middle of the 20th century, when interstate commerce was far less extensive than it is today. Respondents, however, are not the prototypical "local" pharmacist; between 60% and 95% of respondents' total sales of compounded drugs are to out-of-state customers. See Compl. ¶ 26 (C.A.E.R. 7).

Because pharmacies likewise are not exempt from the FDCA's misbranding and adulteration provisions, those provisions also applied to compounding by pharmacies. Compounded drugs of the sort traditionally created by pharmacies are prescription drugs. The FDA has interpreted the FDCA to provide that all unapproved prescription drugs are misbranded, and the lower courts have sustained that interpretation. See, *e.g.*, *United States* v. *Articles of Drug*, 625 F.2d 665, 673, 675 (5th Cir. 1980); *United States* v. *Baxter Healthcare Corp.*, 712 F. Supp. 1352, 1359 (N.D. Ill. 1989), aff'd, 901 F.2d 1401 (7th Cir. 1990); see also *Algon Chem.*, *supra* (applying this interpretation to bulk drugs to be used as components of compounded veterinary drugs); *9/1 Kg. Containers*, *supra* (same).

Under 21 U.S.C. 352(f)(1), a drug is misbranded unless its labeling bears "adequate directions for use," which the FDA has long defined to mean "directions under which the layman can use a drug safely and for the purposes for which it is intended." See 17 Fed. Reg. 6818 (1952) (promulgating 21 C.F.R. 201.5); *Alberty Food Prods.* v. *United States*, 194 F.2d 463, 464 (9th Cir. 1952). The FDA has determined that directions under which the layperson can use a drug safely cannot be written for an *approved* prescription drug because such drugs, by definition, are "not safe for use except under the supervision of a practitioner licensed by law to administer" them, 21 U.S.C. 353(b)(1)(B) (1994 & Supp. V 1999), and are therefore unsuitable for self-medication. See *Articles of Drug*, 625 F.2d at 672-673. In the case of *unapproved* new drugs, adequate directions for use cannot be written as a matter of law, even by a physician. See *Algon Chem.*, 879 F.2d at 1159-1161 (explaining that the FDCA was intended to control the availability of drugs for prescribing by physicians, and prescriptions for compounded drugs that are unapproved new drugs are not exempted from the Act as an aspect of the practice of medicine) (citing *United States* v. *Rutherford*, 442 U.S. 544 (1979)); *9/1Kg. Containers*, 854 F.2d at 176-177 (also citing *Rutherford*).[3]

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[3] The FDCA provides an exemption from the requirement that drugs contain adequate directions for use for "[a]ny drug dispensed by filling or

In addition, before enactment of FDAMA, compounded drugs and their components often would have been considered adulterated under the FDCA, because a drug is adulterated whenever it is "manufacture[d], process[ed], pack[ed], or h[eld]" under methods, facilities or controls that "do not conform to or are not operated or administered in conformity with current good manufacturing practice." 21 U.S.C. 351(a)(2)(B) (1994 & Supp. V 1999). FDA regulations (21 C.F.R. Parts 210 and 211) establish the minimum requirements. Because those requirements were stringent, especially as they developed over time, compliance with them was costly, and most pharmacy compounding processes and facilities would not have complied.

The FDCA prohibits "the doing of any * * * act with respect to, a * * * drug * * *, if such act is done while such article is held for sale (whether or not the first sale) after shipment in interstate commerce and results in such article being adulterated or misbranded." 21 U.S.C. 331(k). The definition of drug includes not only the finished product itself, but also its components. 21 U.S.C. 321(g)(1)(D). Thus, if a drug or one of its components had been shipped in interstate commerce, and the drug or its components became adulterated or misbranded while the drug or the components were held for sale after that shipment, Section 331(k) was

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refilling a written or oral prescription of a practitioner licensed by law to administer such drug." 21 U.S.C. 353(b)(2). That exemption, however, applies only at the time the drug is "dispensed." Thus, when compounded drugs are prepared in advance of dispensing, for example "in limited quantities before the receipt of a valid prescription order for such individual patient," 21 U.S.C. 353a(a)(2)(A) (Supp. V 1999), they lack adequate directions for use, and thus are misbranded unless they qualify for a regulatory exemption from the adequate-directions-for-use requirement. See 21 U.S.C. 352(f) (authorizing Secretary to exempt drugs from that requirement); 21 C.F.R. 201.100 *et seq.* (exemptions). Unapproved new drugs that are not intended solely for investigational use do not qualify for any of the regulatory exemptions. See *ibid.*

violated. See, *e.g.*, *Baker* v. *United States*, 932 F.2d 813, 814-815 (9th Cir. 1991); *United States* v. *Dianovin Pharm., Inc.*, 475 F.2d 100, 103 (1st Cir.), cert. denied, 414 U.S. 830 (1973).

It was against the background of those statutory provisions and the FDA announcement and implementation of its enforcement policy in 1992 (see Pet. App. 71a; *Professionals & Patients*, 56 F.3d at 593-594, 599) that Congress enacted Section 353a to specify in the FDCA itself the circumstances in which compounding by pharmacists would be lawful under the FDCA. Section 353a reflected "extensive" consultation by committees of Congress with the FDA and other interested parties to reach a consensus on how "to ensure the continued availability of compounded drugs as a component of individualized therapy, while limiting the scope of compounding to prevent manufacturing under the guise of compounding." H.R. Conf. Rep. No. 399, 105th Cong., 1st Sess. 94 (1997); accord S. Rep. No. 43, 105th Cong., 1st Sess. 67 (1997). As enacted by Congress, Section 353a responds to the application of the new drug approval, misbranding, and adulteration provisions of the FDCA, as described above, by exempting pharmacy compounding from Sections 355 (new drug approval), 352(f)(1) (adequate directions for use) and 351(a)(2)(B) (good manufacturing practice) of Title 21 if the compounding complies with the conditions in Section 353a.

iv. Even if drugs compounded in the ordinary practice of pharmacy were exempt from the premarket approval requirements, the government still would have a substantial interest in preventing abuse of that exemption by pharmacies engaged in compounding that *exceeds* the ordinary practice of pharmacy and is tantamount to manufacturing. Pharmacies that engage in such activity directly circumvent the new drug approval process and undermine the incentives for traditional manufacturers to comply with that process. Section 353a's solicitation and advertising conditions are well

calibrated to that interest, because a pharmacy that is compounding without complying with those conditions is not engaged in the ordinary practice of pharmacy, which as described above, does not include advertising or promoting particular compounded drugs. See pp. 3, 4-5, *supra*.

2. Section 353a Directly And Materially Advances The Government's Interests

Respondents contend (Br. 25-32) that Section 353a does not directly and materially advance the government's interests. Much of respondents' argument (Br. 26-29, 30-32) is devoted to demonstrating that Section 353a does not advance a supposed governmental interest in reducing demand for compounded drugs. The government's interest is *not*, however, in suppressing demand for compounded drugs. See Pet. Br. 38. The government's interest is in balancing the competing goals of protecting the integrity of the drug approval process and preserving the availability of compounding by pharmacists in response to individual medical needs. Thus, the government seeks to ensure that a compounded drug is subjected to premarket approval when demand is or may be widespread and advertising could channel demand to that unapproved new drug.

Respondents' arguments that advertising does not drive demand for compounded drugs because physicians act as a brake (Br. 28), that advertising generally only channels and does not create demand (Br. 29), and that this Court and other courts have rejected prohibitions on advertising as a means of suppressing demand (Br. 26-28) are thus beside the point. In any event, there is support in this Court's cases for the common-sense proposition that advertising stimulates demand as well as channels it. See *Lorillard Tobacco Co.* v. *Reilly*, 533 U.S. 525 (2001); *Central Hudson*, 447 U.S. at 567-569; *United States* v. *Edge Broad. Co.*, 509 U.S. 418, 434 (1993). *Posadas de Puerto Rico Assoc.* v. *Tourism Co.*, 478 U.S. 328, 341-342 (1986). This common-sense proposition

would seem to apply to physicians as well. J. Avorn, *et al.*, *Scientific versus Commercial Sources of Influence on the Prescribing Behavior of Physicians*, 73 Am. J. of Med. 4, 6 (July 1982) ("Physicians who held advertising-oriented beliefs about the index drugs were generally unaware that they were strongly influenced by non-scientific sources.").

The FDAMA provisions that respondents assert undermine the government's interest (Br. 30-32) do not undermine the government's *actual* interest in preventing manufacturing of unapproved new drugs under the guise of compounding. FDAMA permits a pharmacy to advertise its compounding services generally because that kind of advertising does not suggest the existence of, or foster the growth of, a market for any *particular* compounded drug. Such advertising therefore does not distort the incentives of drug manufacturers to comply with the new drug approval provisions. At the same time, advertising of compounding services promotes the governmental interest in preserving the availability of pharmacy compounding in response to individual medical needs. Pet. Br. 40. Likewise, the absence of more stringent volume limitations on the *aggregate* distribution of compounded drugs does not undermine the advertising and solicitation provisions, which are designed to prevent compounding without premarket approval of a *particular* drug that is tantamount to manufacturing. *Id.* at 41.

3. Section 353a Is No More Extensive Than Necessary To Further The Government's Interests

Respondents also contend (Br. 13, 32-33) that Section 353a's advertising and solicitation provisions are more extensive than necessary to accomplish the government's aims. Respondents argue (Br. 32-33) that disclaimers could prevent consumers from being misled into believing that compounded drugs are FDA-approved. They do not explain, however, how disclaimers are consistent with the goal of

preserving the integrity of the new drug approval provisions. Instead, respondents suggest (Br. 13) that the government's concern about the new drug approval process is misplaced because compounded drugs are not subject to preapproval. As discussed above, however, that suggestion is incorrect. See pp. 6-15, *supra*. Respondents' contention (Br. 44) that a physician prescription provides adequate protection for patients who receive compounds suffers from a similar flaw. The very premise of the FDCA, based on decades of experience, is that physician screening is not sufficient to protect against the risks of widespread distribution of drugs that have not been proven safe and effective. See Pet. Br. 20-23.

Respondents suggest (Br. 45) that Section 353a's advertising and solicitation provisions are unnecessary to safeguard the new drug approval process because the FDA can take enforcement action against a pharmacy that threatens that process by operating beyond the ordinary practice of pharmacy. According to the NABP itself, however, solicitation or advertising of specific compounded drugs *is* activity outside the ordinary practice of pharmacy. See p. 5, *supra*. Moreover, the FDA historically considered whether a pharmacy was engaging in promotional activity in determining whether the pharmacy was exceeding the bounds of ordinary pharmacy practice. Pet. Br. 6, 32-33.

Respondents also incorrectly contend that the solicitation and advertising provisions are more extensive than necessary because they are "absolute restrictions upon truthful speech" and "prevent the very types of advertisement and promotion that this Court held could not be restricted in other cases." Resp. Br. 33 (citing *44 Liquormart, Inc.* v. *Rhode Island*, 517 U.S. 484 (1996), *Rubin* v. *Coors Brewing Co.*, 514 U.S. 476 (1995), and *Virginia State Bd. of Pharmacy*, *supra*). Section 353a does *not* absolutely prohibit any speech. A pharmacy that wishes to mass-produce a particular drug and promote that product by advertising may do so—just as any other manufacturer may—if it complies with the FDCA's new drug approval and related requirements. It is only if the pharmacy desires to avail itself of the exemption from those otherwise generally applicable requirements that it must limit its promotional activities. Moreover, even when a pharmacy takes advantage of the exemption, it is permitted to advertise its compounding services generally. 21 U.S.C. 353a(c) (Supp. V 1999). Section 353a's advertising and solicitation provisions are thus significantly less onerous than the absolute prohibitions on speech involved in *44 Liquormart*, 517 U.S. at 489-490 (categorical ban on advertisement of alcohol prices); *Coors Brewing*, 514 U.S. at 480-481 (prohibition on disclosure of alcohol content on beer labels); and *Virginia State Board of Pharmacy*, 425 U.S. at 752 (effective prohibition on advertising or other affirmative dissemination of all prescription drug price information).

Finally, respondents contend (Br. 46-48) that, even if compounded drugs are subject to the new drug approval requirements, the First Amendment categorically prohibits conditioning an exemption from such a generally applicable requirement on relinquishment of First Amendment rights. But, to the extent that pharmacy compounding violated the FDCA before FDAMA was enacted (see pp. 12-15, *supra*), respondents had no First Amendment right to advertise the sale of compounded drugs. See *Pittsburgh Press Co.* v. *Human Relations Comm'n*, 413 U.S. 376, 388 (1973). They therefore were not required to relinquish any First Amendment right in exchange for the benefit of the exemption.

In any event, respondents' contention is not correct. Respondents rely on the plurality opinion in *44 Liquormart*. See Resp. Br. 46-47 (citing 517 U.S. at 510-514 (opinion of Stevens, J., joined by Kennedy, Thomas, and Ginsburg, JJ.)). That opinion, however, did not state that the government

may *never* condition an exemption from a generally applicable requirement on the beneficiary's agreement to a speech limitation. The opinion merely rejected the argument that the "greater" power to deny the exemption altogether *always* legitimizes the "lesser" power to condition the exemption on the surrender of First Amendment rights. See 517 U.S. at 510-513. Such a condition is subject to scrutiny under the Court's unconstitutional conditions doctrine, but that scrutiny is no more demanding than the *Central Hudson* test. See *Dolan* v. *City of Tigard*, 512 U.S. 374, 385, 391 (1994) (noting that government may not condition benefit on relinquishment of a constitutional right unless waiver of right is reasonably related to benefit and citing First Amendment cases). As explained above and in our opening brief, the solicitation and advertising condition on the exemption provided by Section 353a satisfies scrutiny under *Central Hudson*.

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For the foregoing reasons, and the reasons stated in our opening brief, the judgment of the court of appeals should be reversed, and the case should be remanded with instructions to enter judgment for the petitioners.

Respectfully submitted.

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